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Age-Related Patterns in Clinical Presentations and Gluten-Related Issues Among Children and Adolescents With Celiac Disease

Pornthep Tanpowpong, MD, MPH¹, Sarabeth Broder-Fingert, MD¹, Aubrey J. Katz, MD¹ and Carlos A. Camargo Jr, MD, DrPH²

OBJECTIVES: Celiac disease (CD) is common and often cited as an “iceberg” phenomenon (i.e., an assumed large number of undiagnosed cases). Recently, atypical or asymptomatic manifestations are becoming more commonly described in older children and adolescents. Moreover, CD diagnosis in children can be complicated by several factors, including its diverse clinical presentations, delay in recognizing CD signs and symptoms, and premature dietary gluten avoidance before the formal diagnosis of CD. To date, few studies have directly examined age-related differences in clinical characteristics and gluten-related issues among children with CD. The aim of this study was to determine age-related patterns in clinical characteristics and gluten-related issues among children with confirmed CD.

METHODS: We performed a structured medical record review of biopsy-proven CD patients, aged 0–19 years, between 2000 and 2010 at a large Boston teaching hospital. Data collection included demographics, medical history, gluten-related issues, and diagnostic investigations (CD-specific serology, upper gastrointestinal endoscopy, and small intestinal biopsy). The first positive duodenal biopsy with Marsh III classification defined age of diagnosis. Patients were divided into three age groups for comparisons of the aforementioned characteristics: infant-preschool group (0–5 years), school-aged group (6–11 years), and adolescence group (12–19 years).

RESULTS: Among 411 children with biopsy-proven CD, the mean age was 9.5 (s.d. 5.1) years. Most were female (63%) and white (96%). All children had positive CD-specific serology. Most children presented with either abdominal complaints or bowel movement changes. Overall, boys were more common among infant-preschool group compared with the other age groups. More distinct clinical manifestations (vomiting, bowel movement changes, and weight issues) were apparent in the youngest group, whereas school-aged children had more subjective abdominal complaints at the initial presentation. Conversely, the adolescents were most likely to present without any gastrointestinal (GI) symptoms, but not when this was combined with absence of weight issues. Age of diagnosis was not associated with atypical extraintestinal CD presentations. Regarding the gluten-related issues, 10% of school-aged children avoided dietary gluten before the formal CD diagnosis, and 27% of the adolescents reported dietary gluten transgression within the first 12 months of diagnosis, significantly higher than the other age groups. Age differences in histopathology were also found. Whereas the infant-preschool group had a higher proportion of total villous atrophy, the older children were more likely to have gross duodenal abnormalities and chronic duodenitis suggestive of CD at the time of diagnosis.

CONCLUSIONS: Children and adolescents with CD have age-related patterns in both the clinical presentations and gluten-related issues. More pronounced clinical and histological features were determined in younger children, whereas older children more commonly presented with solely subjective abdominal complaints or even without any GI symptoms. However, silent and atypical extraintestinal CD presentations were comparable between age groups. In addition to the aforementioned presentations, the higher rates of dietary gluten avoidance and transgression in older children make CD diagnosis and management particularly challenging. These age-related patterns may further increase awareness, facilitate early diagnosis, and improve patient care of pediatric CD.

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INTRODUCTION

Celiac disease (CD) is a genetically determined autoimmune enteropathy with a recognized trigger of gluten and related proteins.¹ Several studies report significant increases in

disease prevalence in the past two decades with an approximate prevalence of 1% in recent population screening efforts among both children and adults in industrialized countries;^{2,3} this prevalence makes CD one of the most common lifelong diseases in humans. Increased awareness

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in the community and among health-care providers on CD in conjunction with sensitive serologic markers (tissue transglutaminase antibody and endomysial antibody) for screening high-risk patients enhance the diagnostic yield.^{1,4} However, even with highly sensitive and specific investigations, substantial numbers of undiagnosed CD cases remain common in the pediatric population.^{2,5} Nowadays, CD children have been diagnosed at a much later age compared with the previous decades, which could partly be because of absent or minimal symptoms at the initial presentation in the older children and adolescents and smaller proportion of children with classic CD presentation.⁶

Moreover, anecdotal evidence suggests that gluten avoidance is relatively common among the population without prior diagnosis of confirmed CD. We recently found that the prevalence of CD in New Zealand children who avoided gluten was five times higher than the actual doctor-diagnosed CD (5% vs. 1%, respectively).⁷ Therefore, making a definite diagnosis of CD could be even more challenging in patients who present with atypical or asymptomatic manifestations and/or avoid dietary gluten before the proper diagnostic evaluations (i.e., serology and intestinal biopsy).⁸ To date, few studies have directly examined age-related clinical presentations and gluten-related issues among children with CD. Our aim was to study this issue in a well-characterized group of children and adolescents with positive CD-specific serology and biopsy-confirmed CD.

METHODS

We created a database of CD patients between January 2000 and December 2010 at the Massachusetts General Hospital, a large Boston teaching hospital and referral center. Potential cases were initially identified using ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification), code 579.0, which includes celiac disease, celiac crisis, gluten enteropathy, and nontropical sprue. Then, structured medical record reviews were performed using a data abstraction form that included demographic data (age, gender, and race/ethnicity) and information during health-care encounters (initial presenting signs and symptoms, patient- or parent-reported comorbid conditions, and family history of CD and CD-related conditions). We collected information regarding gluten-related issues including dietary gluten avoidance before the CD diagnosis (yes/no) and dietary gluten transgression verified by a dietitian within the first 12 months of CD diagnosis and a formal physician's recommendation to implement gluten-free diet (yes/no).

Data on serologic markers, upper endoscopy, and biopsy with histopathological information were also gathered. We categorized children into three age groups: infant-preschool group, 0–5 years; school-aged group, 6–11 years; and adolescence group, 12–19 years. At our institution, we used cutoff values of 20 U/ml for tissue transglutaminase antibody positivity and any positive titers for endomysial antibody positivity. According to the recent ESPGHAN CD guideline,⁴ most commercially available kits for tissue transglutaminase antibody applied the cutoff values between 3 and 20 U/ml; we believe that applying 20 U/ml cutoff would limit the false

positive results. Small intestinal biopsy suggestive of Marsh III CD was based on the Marsh–Oberhuber classification^{9,10} with a reported degree of villous atrophy: partial, IIIa; subtotal, IIIb; total, IIIc. The medical records were independently reviewed by two physicians. The study was approved by the institutional review board at our institution.

Biopsy-proven CD patients and age of CD diagnosis.

Date of CD diagnosis was defined at the first histopathological change with increased intraepithelial lymphocytes, crypt hyperplasia, and villous atrophy from the duodenum, which correlates with Marsh III classification for the diagnosis of CD. According to the then-current guideline, confirmation of the diagnosis for pediatric CD still requires small intestinal biopsy.⁸

Biostatistical analysis. We used STATA statistical software 11.1 (StataCorp, College Station, TX). Subjects were described using descriptive statistics, such as mean (s.d.), median (interquartile range), and proportion (with 95% confidence interval). Comparisons of discrete variables across different age groups were assessed using χ^2 tests or Fisher's exact tests, when appropriate. For the continuous variables, we used analysis of variance tests. A two-sided $P < 0.05$ was considered statistically significant.

RESULTS

We identified 411 patients with biopsy-proven CD. All patients with biopsy-proven CD had a documentation of positive CD serology (either tissue transglutaminase antibody or endomysial antibody). Baseline characteristics are shown in Table 1. Age of CD diagnosis ranged from 11 months to 19 years, with 119 (29%) from the infant-preschool age group, 148 (36%) from the school-age group, and 144 (35%) from the adolescent group. The vast majority of our patients (99%) were evaluated by the pediatric gastroenterologists before the formal diagnosis of CD. As a large teaching hospital, we also received patients with confirmed positive small intestinal biopsy for CD before the referral from outside institutions (8%) for further evaluation and management.

Overall, most children had subjective abdominal complaints or bowel movement changes. More than 40% of the children had weight issues (weight loss or poor weight gain). We found that 12% had neither gastrointestinal (GI) symptoms nor weight issues. The proportions of children with atypical extraintestinal presentations were: fatigue or malaise, 12%; short stature or stunted height, 5%; iron deficiency (with or without anemia), 3%; and elevated liver enzymes, 2%.

Regarding the past medical history, CD children were also found to have type 1 diabetes in 6%, food allergy in 4%, hypothyroidism in 3%, and Down syndrome in 2%. Immunoglobulin A deficiency (with serum immunoglobulin A level of <7 mg/dl) was found in 10 children, but all underwent intestinal biopsy that confirmed Marsh III lesion in the duodenum. Proportions of reported positive family history (first- and second-degree relatives) of CD, irritable bowel syndrome, and gastroesophageal reflux are shown in Table 1.

Table 1 Baseline demographics and clinical presentations of 411 children with celiac disease, by age of diagnosis

Characteristics	All cases (n = 411)	Age of diagnosis			P value
		0–5 Years (n = 119)	6–11 Years (n = 148)	12–19 Years (n = 144)	
<i>Demographics</i>					
Age of diagnosis, median (interquartile range), years	9.3 (5.3–13.7)	3.3 (2.1–4.9)	8.7 (7.3–10.1)	14.9 (13.5–16.8)	—
		% (95% confidence interval)			
Male, %	37 (32–42)	46 (37–56)	32 (25–41)	33 (26–42)	0.04
Non-Hispanic white, %	96 (94–98)	96 (90–99)	99 (95–100)	94 (89–98)	0.15
<i>Clinical presentations</i>					
Abdominal complaints, % (pain, discomfort, gas, bloating)	60 (55–64)	51 (42–61)	68 (59–75)	56 (47–64)	0.02
Abdominal pain, %	45 (40–50)	27 (19–36)	58 (49–66)	46 (37–54)	<0.001
Abdominal distention, %	9 (7–12)	20 (13–29)	5 (2–11)	4 (1–8)	<0.001
Vomiting, %	20 (15–25)	34 (23–47)	15 (8–23)	15 (8–24)	0.03
Bowel movement changes, %	53 (47–58)	68 (58–77)	50 (41–59)	43 (34–53)	0.001
Diarrhea (without constipation), %	24 (20–29)	31 (22–41)	20 (13–28)	22 (15–31)	0.01
Constipation (without diarrhea), %	20 (16–25)	25 (17–35)	21 (14–29)	16 (9–23)	0.02
Alterations of diarrhea and constipation, %	9 (6–12)	12 (7–21)	9 (4–15)	5 (2–11)	0.02
Weight issues, % (weight loss or poor weight gain)	43 (37–48)	56 (45–67)	34 (25–44)	39 (30–48)	0.006
Diagnosed celiac disease before a referral, %	8 (5–10)	12 (7–19)	3 (1–8)	8 (4–14)	0.03
Absence of gastrointestinal symptoms, %	16 (12–20)	8 (4–15)	16 (11–23)	21 (15–29)	0.02
Absence of gastrointestinal symptoms and weight issues (i.e., silent presentation), %	12 (9–16)	8 (4–14)	12 (7–19)	16 (10–23)	0.14
Atypical extraintestinal presentations ^a , %	20 (16–24)	16 (10–24)	19 (13–27)	24 (17–32)	0.25
<i>Past medical history and family history</i>					
History of food allergy, %	4 (3–7)	7 (3–13)	5 (2–11)	1 (0–5)	0.07
Family history of celiac disease, %	19 (16–23)	12 (7–19)	27 (20–35)	18 (12–25)	0.01
Family history of irritable bowel syndrome, %	8 (6–11)	7 (3–13)	12 (7–19)	5 (2–10)	0.06
Family history of gastroesophageal reflux, %	12 (9–15)	11 (6–18)	13 (8–20)	11 (6–17)	0.81

^aIncluding fatigue/malaise, short stature or stunted height, iron deficiency, and elevated liver enzymes.

We found that 6% of the children and adolescents avoided dietary gluten before the CD diagnosis. Furthermore, 15% of biopsy-confirmed CD patients had gluten transgression within the first year of diagnosis.

Demographics. Age-related patterns of CD manifestations among children of three different age groups are also shown in Table 1. Overall, CD children in the infant-preschool group had a higher male percentage compared with the school-aged and adolescence groups. There were no significant race/ethnicity differences across the three age groups; however, the proportion of non-white patients in the study population was small (4%).

Clinical presentations. Two-thirds of the school-aged group had complaints of subjective abdominal complaints (pain, discomfort, gas, and bloating) at the initial presentation, which was more common than the other two groups. Generally, females more frequently had abdominal pain compared with males with borderline significance (48% vs. 38%, $P = 0.051$). More pronounced GI presentations such as abdominal distention, vomiting, bowel movement changes, or weight issues (weight loss or poor weight gain) were more common in the younger age group. This group also more commonly presented with a prior biopsy-proven CD diagnosis before the referral to our institution. Conversely, the adolescence group had a significantly higher proportion of patients with an absence of GI symptoms. No significant difference was found when comparing male and female patients without GI symptoms (18% vs. 15%, $P = 0.34$).

However, after combining the absence of GI symptoms and absence of weight issues (i.e., silent CD), no statistically significant differences between age groups were found. Moreover, there were no age-related differences in atypical extraintestinal presentations or nonspecific complaints (i.e., poor sleep, poor appetite; all $P > 0.20$). None of our patients had a documented history of dermatitis herpetiformis.

Past medical history and family history. Besides a borderline significant higher rate of history of food allergy among infant-preschool children, no age-related differences were found in other comorbid conditions including type 1 diabetes ($P = 0.27$), hypothyroidism ($P = 0.46$), gastroesophageal reflux ($P = 0.30$), and Down syndrome ($P = 0.37$). Age-related patterns in reported positive family history of CD, irritable bowel syndrome, and gastroesophageal reflux are shown in Table 1. We found significantly higher proportion of school-aged children with reported positive family history of CD, and borderline higher proportion with positive family history of irritable bowel syndrome in the same age group. We also noted that female CD patients were approximately three times more likely to have a family history of irritable bowel syndrome than the male individuals (11% vs. 3% respectively, $P = 0.007$).

Gluten-related issues (dietary gluten avoidance and transgression). A total of 10% of school-aged children avoided dietary gluten before the formal CD diagnosis was made, and this rate was two times higher than the infant-preschool group and five times higher than the adolescence

Table 2 Gluten-related issues and upper endoscopy and small intestinal biopsy findings in celiac disease patients, by age of diagnosis

Characteristics	Data available (n)	All cases	Age of diagnosis			P value
			0–5 Years	6–11 Years	12–19 Years	
<i>Gluten-related issues</i>						
Dietary gluten avoidance before formal celiac disease diagnosis, %	341	6 (4–9)	% (95% confidence interval)			0.02
			5 (2–12)	10 (6–17)	2 (0–6)	
Dietary gluten transgression within the first 12 months after diagnosis, %	384	15 (11–20)	10 (5–18)	9 (4–16)	27 (19–37)	<0.001
<i>Upper endoscopy and small intestinal biopsy</i>						
Documented gross duodenal abnormalities, %	392	68 (63–73)	58 (48–67)	71 (62–78)	74 (65–81)	0.02
Chronic duodenitis on biopsy, %	396	23 (19–28)	17 (10–25)	22 (15–29)	30 (22–38)	0.045
Total villous atrophy (Marsh IIIc), %	411	32 (25–38)	46 (33–59)	27 (17–38)	24 (15–35)	0.02
Increased antral intraepithelial lymphocytes, %	387	10 (7–14)	18 (11–26)	7 (3–12)	8 (3–12)	0.006
Chronic antral gastritis, %	387	32 (26–37)	30 (22–40)	30 (23–38)	35 (27–43)	0.69
Increased eosinophils in the distal esophagus, %	378	12 (9–16)	13 (7–20)	13 (8–19)	12 (7–19)	0.99

group. No children in the study underwent gluten restriction-rechallenge process before the final CD diagnosis was made. Within the first 12 months of CD diagnosis and formal physician's recommendation to implement gluten-free diet, more than a quarter of the adolescence group reported dietary gluten transgression (either intentional or unintentional), which was approximately three times more often than the two younger age groups.

Upper endoscopy and small intestinal biopsy. Almost half (48%) of the children had an abnormal antral biopsy, and 18% had abnormalities in the distal esophageal biopsy, most with increased eosinophils suggestive of reflux injury. The older children were more likely to have gross duodenal abnormalities suggestive of CD (either flat, scalloping, or nodularity) and chronic duodenitis on biopsy at the time of diagnosis (Table 2). On the other hand, both the total villous atrophy (Marsh IIIc) and increased antral intraepithelial lymphocytes were more likely in the infant-preschool group, but proportions of diagnosed lymphocytic gastritis were comparable ($P=0.09$).

DISCUSSION

The iceberg phenomenon of CD (i.e., an assumed large number of undiagnosed cases) remains an important concern in children and adolescents despite increased disease prevalence and awareness, highly sensitive and specific CD serologic markers, and improved accessibility of upper GI endoscopy and biopsy.^{2,5} Atypical or asymptomatic manifestations undoubtedly contribute to this phenomenon by decreased awareness among patients, caregivers, and health-care professionals.¹¹ Moreover, diagnosing CD can be further challenged by premature implementation of dietary gluten avoidance before the definite diagnosis is made.⁸ Anecdotal evidence suggests that gluten avoidance is relatively prevalent in the community, and we recently found that 5% of New Zealand children in the population-based study avoided gluten, whereas the prevalence of diagnosed CD was similar to other industrialized countries (1%).⁷ To date, there is no evidence in the scientific literature to suggest the precise amount of ingested gluten that elicits a measur-

able mucosal response. Moreover, available studies on gluten avoidance in the general population (without prior CD diagnosis) are very limited.

Some previous data exist on the different age-related patterns of CD presentations in children vs. adults. Vivas *et al.*¹² prospectively examined 66 CD children with the mean age of 3.6 years with two-thirds <2 years of age, and most young children presented with more pronounced symptoms and severe villous atrophy. However, the current evidence showed that pediatric CD are diagnosed at a later age with less apparent clinical manifestations.⁶ To our knowledge, this is the first study to directly examine both the clinical presentations and gluten-related issues among pediatric CD patients of different age groups.

Among 411 biopsy-proven CD children and adolescents with positive CD serology, various age-related characteristics were detected; the previous study had suggested that interobserver agreement is substantial when combining positive serology and positive Marsh III biopsy for the CD diagnosis.¹³ Overall, higher male percentage was found in the infant-preschool age group. A simple explanation for this gender difference is elusive but may relate to dissimilar hormonal and immune responses to injury and inflammation in the presence of gluten introduction during early childhood; related gender differences have been observed in other immune system-mediated disorders.^{14,15}

Regarding the clinical manifestations, the school-aged and adolescence groups more frequently presented with non-specific abdominal complaints. Moreover, the absence of GI symptoms was also more commonly noticed in the older children. However, on combining the absence of GI symptoms and absence of weight issues (i.e., silent CD), the statistical significance on the age-related patterns disappeared (Table 1), which differs from earlier studies.^{6,11} Furthermore, no significant differences were found in atypical extraintestinal CD presentations. The proportions of children with iron deficiency and elevated liver enzymes were comparable to the prior study.¹² The infant-preschool group not only had more prominent clinical presentations, similar to prior studies,^{6,12} but also were more likely to be diagnosed with biopsy-proven CD before the referral to our institution. Possible explanations to the latter finding include more

pronounced manifestations that led to an earlier CD diagnosis and tendency to refer patients with more severe presentations to a tertiary care center. Regarding the bowel movement issues, we found that a relatively high percentage (20%) of CD children presented with constipation, compared with prior studies.^{16,17} The infant-preschool group not only had more children with diarrhea (without constipation) but also higher proportions of constipation and alterations of both when compared with the older children (Table 1), although the previous review suggested that constipation is more common in older children and adolescents with CD.¹¹ These disparities might possibly be because of various reporting and/or referral issues by the caregivers and health-care providers, a possibility that requires further investigation. Generally, the younger children could likely have limited capability to express subjective symptoms when compared with the older individuals. Natural courses, environmental factors (e.g., breastfeeding and gluten introduction), and disease pathogenesis could be different between younger and older children.

We found a borderline significant higher proportion of reported food allergy in the youngest group. Both CD and food allergy are prevalent and increasingly diagnosed in children.^{6,18} These two conditions can both present with nonspecific GI symptoms such as vomiting and/or diarrhea in infants and young children.¹⁹ Therefore, health-care providers might initially diagnose these children with presumed food allergy before completing CD evaluation in suspected cases. The significant age-related differences in family history of CD were interesting but difficult to explain. School-aged children and adolescents, who were more likely to have no or less typical CD symptoms, might also be more likely to undergo CD screening solely because of positive family members with CD compared with the younger children. The similar reason might explain the borderline significant higher proportion of family history of irritable bowel syndrome among the school-aged children as well. Another possible explanation might be because of differences in parental or patient reports across the age groups. These questions will need to be addressed with future research.

Notably, we found that dietary gluten avoidance before the formal CD diagnosis is common in children (6%), with the higher proportion among school-aged children up to 10%, although the current CD prevalence is ~1% in the general pediatric population.² As the school-aged group more commonly presented with nonspecific abdominal complaints, caregivers or health-care providers might implement dietary gluten restriction as a therapeutic trial to alleviate these symptoms. Recent evidence suggested that nonceliac gluten intolerance exists in adults.²⁰ Contrary, the adolescents were less likely to avoid gluten before CD diagnosis, which might be because of increased identity, independence, and distinctive peer interaction during this stage of development. The similar grounds could also explain the high rates (27%) of dietary gluten transgression within the first year of CD diagnosis in this age group. An investigation on decisions to implement and continue dietary gluten avoidance among patients, caregivers, and health-care professionals would be valuable to explain these findings.

At the initial CD diagnosis, the more prominent histological features (total villous atrophy (Marsh IIIc) and increased antral

intraepithelial lymphocytes) at diagnosis were found among the infant-preschool group, similar to the prior reports.^{11,12} One study showed that children with increased gastric intraepithelial lymphocytes are more likely to be diagnosed at an earlier age, and present with more pronounced laboratory and duodenal mucosal abnormalities.²¹ The recent study also showed decreased proportions of CD children diagnosed in 2000–2006 with total villous atrophy when compared with individuals who were diagnosed during the previous decade.⁶ On the other hand, older children were more likely to have grossly visible and chronic changes in the duodenum, which might be because of diverse immune responses and histopathological changes between age groups (i.e., timing of CD diagnosis).

This study has some potential limitations. The study was conducted in a retrospective fashion at a large teaching hospital. Although we acknowledge the possibility of incomplete information (e.g., anthropometric data), both recall and information biases as well as the inability to control for *all* of the parent- or patient-reported data with the physicians' interpretation, we believe that our novel findings will provide a platform for the development of age-related approaches for evaluation and management of CD. Prior evidence suggests that delay in CD diagnosis is correlated with the patient's age;¹² in other words, there will tend to be more delay in older children (which might be subject to more recall biases), as compared with younger children. With regard to parental (proxy) reporting, the limited communication abilities of infants and younger children have inevitably restricted expression of subjective symptoms in this group. Therefore, both researchers (and clinicians) need to rely on the parental reports for the clinical presentations of younger children. We are also well aware that cutoff ages for "pediatric" and "adolescent" population can be varied between different geographic areas. We decided to employ 19 years of age as a cutoff year based on social environment and culture on development (according to the Erikson's stage of development) that would mainly be applied to the aforementioned gluten-related issues.

It is noteworthy that all study patients were evaluated before release of the recent 2012 CD guideline,⁴ and we still believe that it was most appropriate to apply the then-current NASPGHAN 2005 guideline, especially in these North American children and adolescents.⁸ We also note that the issue of nonbiopsy diagnosis in CD remains debatable.²² Furthermore, all patients had documentation of both positive CD-specific serology and biopsy, as we believe, in this situation, that genetic markers would not play an important role in assisting CD diagnosis.^{4,8} The data on gluten-related issues were obtained in a qualitative way (yes/no) from the medical records. As a generally accepted strategy, patients who undergo CD evaluations should consume regular gluten-containing diet while obtaining serology and biopsy to increase the yield of diagnosis and limit potential false negative results.⁸ Gluten avoidance can also result in several disadvantageous effects on the quality of life,²³ self-perceived health,²⁴ psychosocial dynamics,²⁵ nutritional status,²⁶ and increased economic health burden.²⁷ Moreover, the proportions of dietary gluten transgression in our study were comparable to most previous studies.^{28–30} Currently, strict lifelong gluten-free diet remains the only effective management in CD. As a result, the history of gluten restriction before making a definite diagnosis and any

degree of dietary transgression after the diagnosis would be unsuitable in the processes of proper evaluation and management of CD, respectively.

In summary, we describe the age-related patterns in both the clinical presentations and gluten-related issues among children and adolescents with CD. Causal explanations for the observed findings will require further studies that address potentially different disease pathogenesis, diagnostic and referral patterns, and decisions to implement and maintain gluten avoidance by age. We found that whereas the vast majority of children and adolescents presented with subjective abdominal complaints or bowel movement issues, older children more commonly presented with subjective or vague abdominal complaints or an absence of GI symptoms. However, silent (i.e., absence of both GI symptoms and weight issues) and atypical extraintestinal CD presentations were comparable between age groups. Furthermore, premature gluten avoidance before the CD diagnosis in school-aged children and dietary gluten transgression after the CD diagnosis in adolescents were common. These clinical and gluten-related factors make the diagnosis and management of CD in older children particularly challenging. We believe that these age-related patterns may further increase awareness, facilitate early recognition and diagnosis, and improve patient care of pediatric CD.

CONFLICT OF INTEREST

Guarantor of the article: Carlos A. Camargo Jr, MD, DrPH.

Financial support: None.

Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Celiac disease (CD) is one of the most common lifelong disorders in children.
- ✓ “Iceberg” phenomenon also remains a major problem in children, and may result from atypical or even asymptomatic manifestations.
- ✓ Recent study showed high rates of children who avoided gluten without diagnosed CD.
- ✓ Few studies have directly examined age-related patterns in both the clinical presentations and gluten-related issues among children and adolescents with CD.

WHAT IS NEW HERE

- ✓ Most children present with either subjective abdominal complaints or bowel movement changes.
- ✓ Although older children are more likely to present nonspecific abdominal complaints, the frequency of silent and atypical extraintestinal CD presentations does not differ by age.
- ✓ High rates of gluten avoidance before CD diagnosis are noted in school-aged children.
- ✓ Diagnosing and managing CD in the older children may be more challenging.

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